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Helsinki, 12 April 2018

Substance name: a mixture of: 4-(2,2,3- trimethylcyclopent-3-en- 1-yl)-1-methyl-2-oxabicyclo[2.2.2]octane; 1-(2,2,3- trimethylcyclopent-3-en- 1-yl)-5-methyl-6-oxabicyclo[3.2.1]octane; spiro[cyclohex-3-en-1-yl- [(4,5,6,6a-tetrahydro- 3,6',6',6'a-tetramethyl)- 1,3'(3'aH)- [2H]cyclopenta[b]furan]; spiro[cyclohex-3-en-1-yl- [4,5,6,6a-tetrahydro- 4,6',6',6'a-tetramethyl)- 1,3'(3'aH)- [2H]cyclopenta[b]]furan]

EC number: 422-040-1
CAS number: 426218-78-2
Date of latest submission(s) considered[1]: 13 February 2017
Decision/annotation number: Please refer to the REACH-IT message which delivered this communication (in format SEV-D-XXXXXXXXXX-XX-XX/F)
Addressee(s): Registrant(s)[2] of a mixture of: 4-(2,2,3- trimethylcyclopent-3-en- 1-yl)-1-methyl-2- oxabicyclo[2.2.2]octane; 1-(2,2,3- trimethylcyclopent-3-en- 1-yl)-5-methyl-6-oxabicyclo[3.2.1]octane; spiro[cyclohex-3-en-1-yl- [(4,5,6,6a-tetrahydro- 3,6',6',6'a-tetramethyl)- 1,3'(3'aH)- [2H]cyclopenta[b]furan]; spiro[cyclohex-3-en-1-yl- [4,5,6,6a-tetrahydro- 4,6',6',6'a-tetramethyl)- 1,3'(3'aH)- [2H]cyclopenta[b]]furan] (Registrant(s))

DECISION ON SUBSTANCE EVALUATION

Based on Article 46(1) of the REACH Regulation (Regulation (EC) No 1907/2006), you are requested to submit the following information:

1. **Aerobic Mineralisation in Surface Water – Simulation Biodegradation Test, test method: OECD TG 309, with the registered substance, at a temperature of 12°C, and including the identification and persistency assessment of degradation products.** The degradation half-lives shall be determined for the relevant fractions as further specified in the Appendix 1. The simulation study must be performed using radio-labelled test substance and a mass-balance has to be included. The radio-labelling shall be at the most stable part of the molecules.

If based on the outcome of request 1, one or more of the relevant fractions fulfil the criteria for persistent (P) or very persistent (vP) according to Annex XIII of REACH, the following testing is required:

2. **Bioaccumulation in Fish: Aqueous and Dietary Exposure. Test method: OECD TG 305, with the registered substance.** Separate BCF values must be determined for the relevant fractions as further specified in Appendix 1. Aqueous exposure route must be used.

[1] This decision is based on the registration dossier(s) at the end of the 12-month evaluation period

[2] The terms registrant(s), dossier(s) or registration(s) are used throughout the decision, irrespective of the number of registrants addressed by the decision.

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If based on the outcome of requests 1 and 2, one or more of the relevant fractions fulfil the criteria for vPvB according to Annex XIII of REACH, no further testing is required.

If based on the outcome of requests 1 and 2, one or more of the relevant fractions fulfil the criteria for PB, vPB or PvB according to Annex XIII of REACH, the following testing is required:

3. **Long-term toxicity to aquatic invertebrates, test method: OECD TG 211, *Daphnia magna* Reproduction Test** with the relevant fraction that fulfils the criteria for PB, vPB or PvB and has the highest BCF value based on the outcome of requests 1 and 2.

If based on the outcome of request 3 and other relevant available data it is not possible to conclude whether the relevant fraction meets the criteria for toxic (T) according to Annex XIII, the following testing is required:

4. **Long term toxicity to fish, test method: OECD 210, Fish Early Life Stage Toxicity Test** with the relevant fraction that fulfils the criteria for PB, vPB or PvB and has the highest BCF value based on the outcome of requests 1 and 2.

You have to provide an update of the registration dossier(s) containing the requested information, including robust study summaries and, where relevant, an update of the chemical safety report by **20 January 2020** if only test 1 needs to be performed.

You have to provide an update of the registration dossier(s) by **19 October 2020** if only tests 1 and 2 need to be performed.

You have to provide an update of the registration dossier(s) by **19 July 2021** if only tests 1, 2 and 3 need to be performed.

You have to provide an update of the registration dossier(s) by **19 July 2022** if all requested tests need to be performed.

In addition to the robust study summaries, you shall submit the full study reports for the requirements 1 and 2 by the same deadlines.

The deadlines take into account the time that you may need to agree on which of the registrant(s) will perform the required tests. It has been set to allow for sequential testing or other sequential information gathering or information generation approaches, as appropriate.

The reasons of this decision and any further test specifications are set out in Appendix 1. The procedural history is described in Appendix 2. Further information, observations and technical guidance as appropriate are provided in Appendix 3. Appendix 4 contains a list of registration numbers for the addressees of this decision. This appendix is confidential and not included in the public version of this decision.

Who performs the testing?

Based on Article 53 of the REACH Regulation, you are requested to inform ECHA who will carry out the studies on behalf of all registrant(s) within 90 days. Instructions on how to do this are provided in Appendix 3.

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Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has a suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals

Authorised[3] by Leena Ylä-Mononen, Director of Evaluation

[3] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

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Appendix 1: Reasons

Based on the evaluation of all relevant information submitted on a mixture of: 4-(2,2,3-trimethylcyclopent-3-en- 1-yl)-1-methyl-2- oxabicyclo[2.2.2]octane; 1-(2,2,3-trimethylcyclopent-3-en- 1-yl)-5-methyl-6- oxabicyclo[3.2.1]octane; spiro[cyclohex-3-en-1-yl- [(4,5,6,6a-tetrahydro- 3,6',6',6'a-tetramethyl)- 1,3'(3'aH)-[2H]cyclopenta[b]furan]; spiro[cyclohex-3-en-1-yl- [4,5,6,6a-tetrahydro- 4,6',6',6'a-tetramethyl)- 1,3'(3'aH)- [2H]cyclopenta[b]]furan] (hereafter 'the registered substance' or 'substance') and other relevant available information, ECHA concludes that further information is required to enable the evaluating Member State competent authority (evaluating MSCA) to complete the evaluation of whether the substance constitutes a risk to the environment.

In this decision, information to clarify the concern on suspected PBT/vPvB properties is requested. The evaluating MSCA will subsequently review the information submitted by you and evaluate if further information should be requested to clarify the concerns for suspected PBT/vPvB, environmental exposure and high RCRs.

PBT concern:

The concern(s) identified

Based on the available experimental and QSAR data, the substance, its constituents and impurities are not readily biodegradable and thus screen P/vP. In an OECD 123 study with the whole substance ([redacted]), log Kow values in the range of 4.71-5.01 were measured for different peaks identified in a gas chromatogram analysis. Therefore, all constituents and impurities screen B/vB. Based on the available acute toxicity data on fish, aquatic invertebrates and algae, the whole substance does not meet the screening criterion for T but it cannot be excluded that some of the constituents and/or impurities fulfil the definitive criteria for T. Consequently, there is a concern that some of the constituents or impurities of the substance may have PBT/vPvB properties. This causes a potential risk for the environment as the substance has wide dispersive uses and there is potential for exposure of the environment.

Further information requested under points 1-4 is needed to clarify the PBT concern.

What is the possible regulatory outcome?

Where the new data, once obtained, confirms that the registered substance (or a relevant degradation product) meets the PBT or vPvB criteria, it will allow authorities to consider further regulatory risk management in the form of identification as a Substance of Very High Concern in accordance with REACH Article 57.

Testing approach

According to Annex XIII of REACH, the PBT assessment has to take account of all relevant constituents of the substance. ECHA Guidance on Information Requirements and Chemical Safety Assessment Chapter R.11: PBT/vPvB assessment (Version 3.0, June 2017) describes relevant constituents as all constituents, impurities and additives present in the substance at levels equal or above 0.1 % (w/w). The registered substance is a multi-constituent substance. Based on the registration information, it contains four main constituents and several impurities. The identified constituents and impurities of the registered substance are all structurally similar with each other as they are different enantiomers or isomers of the same structures. Therefore, they are expected to be

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relatively similar with regard to their potential PBT properties.

In a recent OECD 123 study performed with the whole substance ([redacted]), log Kow values of the different peaks detected in a gas chromatogram analysis ranged from 4.71 to 5.01. Furthermore, the KOWWIN QSAR model predicts that two of the impurities, which are very similar to each other, could have slightly higher log Kow values than the other constituents and impurities. Hence, there seems to be some differences between the n-octanol affinity of the constituents and impurities. This means that there may also be differences in the bioaccumulation potential. As the difference in the log Kow values is quite small, also the differences in the BCF values can be expected to be relatively small. However, information on the bioaccumulation of different constituents/impurities is needed in order to be able to draw a firm conclusion. This is because given that the concentrations of the different constituents and impurities range from 5% to 52% and there is no information on the concentration of those constituents/impurities with higher log Kow, determining only one BCF for the whole substance might underestimate the BCF for these constituents/impurities if their concentration is low and the main part of the substance consists of constituents with lower log Kow. Especially in the case where the BCF determined for the whole substance would be close to the B criteria, a concern on the potential B-status of the constituents/impurities with the highest log Kow could remain.

In a comment to a proposal for amendment (PfA) you indicated that the block method can be applied in the assessment of the substance based on the structural similarity of the constituents and impurities. ECHA agrees with you since according to the ECHA Guidance on Information Requirements and Chemical Safety Assessment Chapter R.11: PBT/vPvB assessment (Version 3.0, June 2017) a "fraction profiling (block profiling) approach" can be applied when, due to the complexity of the substance, it is not feasible to fully identify, assess or isolate single constituents but the substance can be divided into fractions/blocks, in which the constituents are structurally similar or in which the constituents are to such an extent similar that their degradation, bioaccumulation and toxicity properties can be expected to follow a regular predictable pattern. ECHA acknowledges that some of the constituents and impurities of the registered substance are very similar to each other, e.g. different stereoisomers of the same structures. Therefore, making the chemical analysis separately for all the constituents and impurities present at a concentration relevant for the PBT assessment could be technically very challenging e.g. due to problems related to their isolation. Therefore, ECHA has decided to use a testing approach to clarify the PBT concern where information is requested for all the relevant fractions of the registered substance. The peaks that can be identified for the registered substance in a gas chromatogram and that have a concentration relevant for the PBT assessment (i.e. ≥ 0.1 % w/w) are referred as relevant fractions.
First, the registered substance will be tested in a simulation degradation study (request 1). The degradation half-lives shall be determined for the relevant fractions. If one or more of the fractions is concluded to be P or vP, the registered substance will be tested in a bioaccumulation study and the BCF values must be determined separately for the relevant fractions. If one or more of the relevant fractions fulfill the criteria for P/vP and B/vB (but not vPvB) the relevant fraction having the highest BCF value based on the outcome of request 2 (bioaccumulation) will be tested in the requested aquatic toxicity studies (requests 3 and 4). You have to justify your choice for the worst-case fraction to be used in these tests. However, if your justification is deemed to be insufficient and ECHA would have a doubt on the worst case scenario, further information on the other constituents or impurities could be requested in future Substance Evaluation decisions.

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Normally, in order to avoid unnecessary vertebrate testing, the assessment to clarify PBT concern starts with the confirmation of persistency followed by bioaccumulation testing. This approach was used in the initial draft decision. In your comments on the draft decision you stated that it seems very probable that the constituents and impurities of the substance will meet the criteria for persistency but it seems more uncertain whether they can meet the criterion for bioaccumulation. Therefore, in your opinion starting the assessment with the bioaccumulation test would be the most cost-effective way forward to clarify the PBT concern. In the draft decision referred to the other Member States and ECHA, such a reverted testing order was applied.

Two Member States competent authorities commented in their PfAs that there is no adequate justification to deviate from the standard testing order since the reverted order is based only on cost grounds without consideration of animal welfare. Such an approach is contrary to the aims of the REACH regulation and ECHA R11 PBT guidance according to which the standard order should normally be followed in order to avoid unnecessary vertebrate testing and a deviation from this is possible only if it can be duly justified. This could be e.g. if there are major practical or technical feasibility issues justifying a reverted order. This does not seem to be the case for the registered substance. Furthermore, based on the available information it is not possible to conclude on the persistence or bioaccumulation, and so the possible time effectiveness of the reverted order is not known.

ECHA agrees that there is no adequate justification for the reverted order, and hence, the standard testing order is used in this decision due to animal welfare considerations.

1. **Aerobic Mineralisation in Surface Water – Simulation Biodegradation Test, test method: OECD 309, at a temperature of 12°C, and including the identification and persistency assessment of degradation products**

Why new information is needed

The hydrolytic half-lives of the whole substance at environmentally relevant pH values are 22-35 days at 25°C based on an OECD 111 study. The substance is not readily biodegradable based on an OECD 301D study and thus screens P/vP. Furthermore, all constituents and impurities screen P/vP based on BIOWIN QSAR predictions.

Information from a simulation biodegradation study is needed to conclude whether the criteria for P/vP in Annex XIII of REACH are met.

This study is to be performed with the registered substance. The degradation half-lives must be determined for the relevant fractions as specified in the above section on testing approach.

Considerations on the test method and testing strategy

The simulation biodegradation study must be conducted following the OECD 309 guideline. The test has to be performed at a temperature of 12°C to represent the average environmental temperature for the EU and has to include the identification of the relevant degradation products, which must be assessed for their potential persistency properties. The simulation study must be performed using a radio-labelled test material and a mass-balance has to be included. The radio-labelling must be done at the most stable part of the molecules.

The amount of suspended solids in the pelagic test should be representative of the level of suspended solids in EU surface water. The concentration of suspended solids in the

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surface water sample used should therefore be approximately 15 mg dw/L. Testing natural surface water containing between 10 and 20 mg SPM dw/L is considered acceptable. Furthermore, if reporting non-extractable residues (NER) in your test results you must explain and scientifically justify the extraction procedure and solvent used obtaining a quantitative measure of NER.

The registered substance is used as test item and the degradation half-lives are to be determined for the relevant fractions.

If the simulation study results in the substance being not P/vP in the tested compartment and these results are sufficient to conclude on persistency in other environmental compartments, no additional simulation tests will be needed. If a concern on the persistency in some of the compartments remains, ECHA can consider whether further simulation testing needs to be requested in future Substance Evaluation decisions.

You shall submit the full study report for the persistency study. Considering the complexity of the case, access to all information available in the full study (i.a. implemented methods, raw data collected, interpretations and calculations, consideration of uncertainties) are needed. This will allow the evaluating MSCA to fully assess the provided information, including the statistical analysis, and to efficiently clarify the concern for persistence.

Consideration of alternative approaches

The request for an OECD 309 test is suitable and necessary to obtain information that will allow to clarify whether one or more of the relevant fractions of the substance meets the criteria for persistency according to Annex XIII of REACH. The persistency is requested to be determined using the OECD TG 309 in order to minimise the formation of NER. The constituents have a high log Koc value and thus adsorption to organic material and high formation of NER can be expected in soil and sediment simulation studies, OECD TG 307 and 308, respectively. This would make the interpretation of results of these tests difficult, as the interpretation of NER is not straightforward and is currently under scientific development.

Consideration of registrants' comments on the draft decision and PfAs

In your comments you agreed that based on the available information the substance screens P/vP and B/vB and therefore further information is needed. You also acknowledged that usually the PBT assessment starts with the confirmation of persistency. However, you argued that in this case starting the PBT assessment with persistency testing would not be the most cost-effective way forward to change the current assumptions on the overall PBT/vPvB properties of the substance as based on the available experimental and QSAR information the constituents and impurities are expected to meet the criteria for persistency in a degradation simulation study but there is more uncertainty on the bioaccumulation potential. Therefore, you proposed to start the assessment with the bioaccumulation study. However, based on the reasoning presented above in the section on the Testing approach, ECHA has decided to use the standard testing order according to the ECHA Guidance R.11.

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Conclusion

Therefore, based on the substance evaluation and in accordance with Article 46(1) of the REACH Regulation, ECHA concludes that you are required to carry out the following study:

Aerobic Mineralisation in Surface Water – Simulation Biodegradation Test, test method: OECD 309, with the registered substance, at a temperature of 12°C, and including the identification and persistency assessment of degradation products. The simulation study must be performed using a radio-labelled test material and a mass-balance has to be included. The radio-labelling shall be at the most stable part of the molecules.

In case degradation products are formed, they have to be identified. Relevant degradation products have to be assessed for their potential persistency.

2. Bioaccumulation in fish: aqueous exposure. Test method: OECD TG 305

Why new information is needed

As explained above, there is a concern that some of the constituents or impurities of the registered substance may have PBT/vPvB properties.

There is no experimental data on the bioaccumulation of the substance or any of its constituents. In a recent partition coefficient study, a weighted average log Kow of 4.79 was determined for the whole substance. Based on the available chromatograms in the study report ([redacted]), the constituents and impurities of the substance have log Kow values in the range of 4.7-5.0. Hence, they all screen B/vB.

KOWWIN QSAR models predicts the same log Kow value of 5.70 for the main constituents and for most of the impurities. For two of the impurities a slightly higher log Kow value of 5.83 is predicted.

In conclusion, there are some differences in the log Kow values of the constituents and impurities and this may lead to differences in the bioaccumulation potential. As the concentrations of the different constituents and impurities are very different, determining only one BCF for the whole substance might underestimate the BCF for some of the constituents/impurities, especially if their concentration is low and the main part of the substance consists of constituents with lower BCF. Especially in the case where the BCF determined for the whole substance would be close to the B criteria, a concern on the B-status of some of the constituents/impurities could remain.

Therefore, further information on the bioaccumulation potential of the different constituents/impurities is needed as based on the currently available information it is not possible to draw any firm conclusion.

Considerations on the test method and testing strategy

The bioaccumulation in fish study must be performed following the OECD TG 305 using the aqueous exposure route. The whole registered substance is to be used as test material and separate BCF values must be determined for the relevant fractions as further specified above in the section on the testing approach.

In the initial draft decision, the choice of the exposure route depended on the outcome of the water solubility test requested initially. In your comments you consider that

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aqueous exposure route is the best option as the concentrations to be used in the OECD 305 study should be at levels at which the substance is soluble in the water phase. In addition, you noted that a dietary study could only be used as part of a Weight of Evidence according to the current ECHA guidance.

ECHA agrees that based on the available information, the aqueous route seems technically feasible for the constituents and impurities of the substance, and this route is normally preferred to the dietary route in the PBT assessment because the resulting BCF can be directly compared with the Annex XIII criteria. Based on the recent OECD 123 study with the registered substance, the log Kow values of the constituents and impurities are in the range of 4.7-5.0. Based on the WSKOW QSAR model, the predicted water solubility of the constituents and impurities is 6.39 and 3.37mg/L when using log Kow of 4.71 and 5.01, respectively, and melting point of -25°C measured for the whole substance as input. The WATERNT QSAR model predicts a water solubility of 4.30 mg/L for the main constituents and most of the impurities, and 6.79 mg/L for two of the impurities. These values are relatively similar with the water solubility of 11.1 mg/L measured for the whole substance in an OECD 105 study using the shake flask method. Therefore, ECHA expects that the water solubility of the constituents and impurities of the substance is in the range of milligrams per litre. Since the concentrations to be used in the OECD 305 test (and in the persistency and aquatic toxicity tests included in this decision) are well below these values, ECHA considers that further information on the water solubility of the worst-case constituent is not needed to be able to decide on the exposure route. Therefore, the request for the water solubility test was removed from the decision and aqueous exposure route is requested for the bioaccumulation test.

You shall submit the full study report for the bioaccumulation study. Considering the complexity of the case, access to all information available in the full study (i.a. implemented methods, raw data collected, interpretations and calculations, consideration of uncertainties) are needed. This will allow the evaluating MSCA to fully assess the provided information, including the statistical analysis, and to efficiently clarify the concern for bioaccumulation.

Consideration of alternative approaches

The request for OECD 305 test is suitable and necessary to obtain information that will allow to clarify whether one or more of the relevant fractions of the registered substance meet the criteria for bioaccumulation according to Annex XIII of REACH. More explicitly, there is no equally suitable alternative way available of obtaining this information. ECHA notes that there is no other experimental test method available at this stage that would generate the necessary information and would not require testing on vertebrate animals.

Consideration of Registrants' comments on the draft decision and PfAs and of the PfAs

In your comments you agreed to perform the bioaccumulation study. However, you proposed to use the whole substance as test material but make the analysis on those constituents that will represent the worst case BCF value. You argued that the small structural differences of the constituents and impurities are not anticipated to cause differences in the bioaccumulation potential, and that the BCF values predicted by the BCFBAF model are well below the 2000 L/kg threshold for both log Kow values of 4.70 and 5.0 when taking into account the biotransformation estimates.

Also two Member States competent authorities proposed in their PfAs to test the whole substance for bioaccumulation.

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In response ECHA points out that although the constituents and impurities are structurally relatively similar, based on the OECD 123 study there are some differences in their log Kow values and this may lead to differences in the bioaccumulation potential. ECHA also notes that based on the BCFBAF v3.01 QSAR predictions performed by the evaluating MSCA, the BCF values (upper, mid and lower trophic level) including biotransformation estimates predicted by the Arnot-Gobas method are above or only slightly below 2000 L/kg when log Kow of 5.0 is used as input and below 2000 when the log Kow of 4.7 is used. Therefore, since the PBT assessment has to consider all relevant constituents and impurities of the substance, in order to be able to draw a firm conclusion on the PBT status of the registered substance, information on the bioaccumulation potential of the different relevant fractions is needed. This will avoid the underestimation of the BCF value of the relevant fractions having the highest log Kow and potential masking of relevant fractions meeting the B criteria in case they are present at low concentrations and most of the substance consists of non-B relevant fractions.

In conclusion, ECHA agrees that the whole registered substance can be used as test item in the bioaccumulation study. However, separate BCF values must be determined for the relevant fractions of the substance.

Conclusion

Therefore, based on the substance evaluation and in accordance with Article 46(1) of the REACH Regulation, ECHA concludes that you are required to carry out the following study:

Bioaccumulation in Fish: Aqueous and Dietary Exposure, Test method: OECD TG 305, with the registered substance. Separate BCF values must be determined for the relevant fractions as further specified above. Aqueous exposure route must be used.

3. Long-term toxicity to aquatic invertebrates, test method: OECD TG 211, Daphnia magna Reproduction Test

Why new information is needed

The need for this study depends on the outcome of the requested simulation biodegradation study (request 1) and the bioaccumulation in fish study (request 2). If one or more of the relevant fractions fulfil the criteria for vPvB according to Annex XIII of REACH, this test is not required. If one or more of the relevant fractions are persistent (P) and bioaccumulative (B) or very bioaccumulataive (vB) OR very persistent (vP) and bioaccumulative (B), this study must be performed.

Based on the available information, the substance does not meet the criteria for T according to Annex XIII of REACH based on human health classification.

There is no long-term toxicity information available on fish or aquatic invertebrates for the registered substance. The only available chronic value of the substance for aquatic organisms is a NOErC of 2.6 mg/L measured for the alga *Pseudokirchneriella subcapitata*. The available acute toxicity values (L(E)C50) of the substance for fish, daphnia and algae are 3.8, 1.3 and 13 mg/L, respectively. Hence, the screening criteria for T is not fulfilled. However, since there is no long-term data, it cannot be excluded that individual constituents or impurities fulfil the definitive criteria for T according to Annex XIII of REACH.

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The ECOSAR (v1.11) QSAR model predicts for the constituents and impurities chronic values of 0.093, 0.101 and 0.496 mg/L for fish, daphnia and algae, respectively, based on the lowest measured log Kow of 4.71. When using the highest measured log Kow of 5.01 as input, the model gives the following chronic values: 0.052, 0.060 and 0.327 mg/L, respectively. However, it is noted that the chronic values predicted by the model for algae are significantly lower than the available experimental NOEC value of the whole substance. This adds uncertainty to the predicted values for fish and daphnia.

In conclusion, based on the QSAR estimations, the constituents and impurities may not fulfil the criterion for T based on aquatic toxicity. However, due to the uncertainties related to the QSAR predictions, it is not possible to firmly conclude on the long-term toxicity of the constituents and impurities to fish and/or aquatic invertebrates based on the currently available information. Therefore, further information on the long-term aquatic toxicity is needed if one or more of the relevant fractions fulfil the criteria for PB, vPB or PvB based on the outcome of requests 1 and 2.

Considerations on the test method and testing strategy

The *Daphnia magna* reproduction test must be performed following the OECD TG 211 guideline.

The test must be performed with the relevant fraction that fulfils the criteria for PB, vPB or PvB and has the highest BCF value based on the outcome of request 1 and 2. You have to justify your selection for the worst-case scenario. However, if the justification is deemed to be insufficient and ECHA would still have a doubt on the worst case scenario, further information on the other fractions could be requested in future Substance Evaluation decisions.

Due to the high tendency to adsorb to organic material and moderate volatility of the constituents and impurities of the substance, the fraction to be tested should be considered a difficult substance for aquatic toxicity testing, and therefore the draft revised guidance OECD TA 23 shall be consulted to help to achieve and maintain the required exposure concentration (OECD TA 23[4]).

The information requested constitutes the first tier in a testing strategy to clarify whether the criterion for T according to Annex XIII of REACH based on long-term aquatic toxicity is met. If based on the requested *Daphnia magna* reproduction study it can be concluded that the fraction tested meets the criterion for T, no further testing is required. In case it is not possible to draw a firm conclusion, long-term testing on fish is required (see request 4).

Consideration of alternative approaches

The request for OECD TG 211 test is suitable and necessary to obtain information that will allow to clarify whether the relevant fraction with the highest BCF meets the criteria for toxicity according to Annex XIII of REACH. If based on the requested toxicity test it is not possible to draw a firm conclusion, long-term testing on fish is requested (request 4).

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[4] OECD Series on Testing and Assessment Number 23, Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO/(2000)6. (Nov 2017 draft revision). http://www.oecd.org/env/ehs/testing/draft-guidance-review-documents-monographs.htm

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Consideration of registrants' comments on the draft decision and PfAs

In your comments you pointed out that the substance does not meet the toxicity criterion at this stage, and you agreed with ECHA that the need for further testing will depend on the outcome of the bioaccumulation study.

Conclusion

Therefore, based on the substance evaluation and in accordance with Article 46(1) of the REACH Regulation, and depending on the outcomes of the simulation biodegradation study (request 1) and the bioaccumulation in fish study (request 2), ECHA concludes that you are required to carry out the following study:
Long-term toxicity to aquatic invertebrates, OECD TG 211. *Daphnia magna* Reproduction Test with the relevant fraction that fulfils the criteria for PB, vPB or PvB and has the highest BCF value based on the outcome of requests 1 and 2.

4. Long-term toxicity to fish, test method 210; Fish Early Life Stage Toxicity Test

Why new information is needed

This testing is only required if one or more of the relevant fractions is considered persistent (P) or very persistent (vP) and bioaccumulative (B) or very bioaccumulative (vB) according to the Annex XIII criteria based on the outcome of requests 1 and 2, and T is not confirmed for the relevant fraction based on the outcome of request 3 (long-term test on invertebrates). If one or more of the relevant fractions is already found to meet the criteria for vPvB and/or PBT in accordance with REACH Annex XIII, this test is not needed, and the request in this decision is therefore conditional. Due to this conditionality, the initial draft decision stated that the long-term toxicity to fish would be requested, if necessary, in a second decision. After your comments the draft decision was modified to include this conditional request in this decision.

As indicated above in the section on the Daphnia reproduction study, no long-term toxicity tests with fish are available for the registered substance or for any of its constituents or impurities. An LC50 of 3.8 mg/L is reported from an acute study with the whole substance. ECOSAR QSAR model predicts chronic values of 0.093 and 0.052 mg/L for fish when using the measured log Kow values of 4.71 and 5.01, respectively, as input.

Hence, the registered substance does not meet the screening criterion for T, and based on QSAR estimations the constituents and impurities may not fulfil the definitive criterion for T either. However, based on the available information no firm conclusion can be drawn on the long-term toxicity to fish of the constituents and impurities. Therefore, further information is needed, if the fraction tested in request 3 is not confirmed to be T based on the outcome of that study.

Considerations on the test method and testing strategy

The long-term toxicity to fish test must be performed following OECD 210 guideline (Fish Early Life Stage Toxicity Test) and using as test item the same fraction that was used in the request 3, i.e., the relevant fraction that meets the criteria for PB, vPB or PvB and has the highest BCF value based on the outcome of requests 1 and 2. You shall justify

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your selection for the worst-case scenario. However, if your justification is deemed to be insufficient and ECHA would still have a doubt on the worst case scenario, further information on other constituents or impurities might be requested in future decisions.

Due to the high tendency to adsorb to organic material and moderate volatility of the constituents and impurities of the registered substance, the fraction to be tested should be considered a difficult substance for aquatic toxicity testing, and therefore guidance shall be consulted to help achieve and maintain the required exposure concentration (OECD TA 23).

Consideration of registrants' comments on the draft decision and PfAs

In your comments you pointed out that the substance does not meet the toxicity criterion at this stage, and you agreed with ECHA that the need for further testing will depend on the outcome of the bioaccumulation study.

Conclusion

Therefore, based on the substance evaluation and in accordance with Article 46(1) of the REACH Regulation, and depending on the outcome of the simulation biodegradation study (request 1), the bioaccumulation in fish study (request 2) and the *Daphnia magna* reproduction study (request 3), ECHA concludes that you are required to carry out the following study using the relevant fraction that meets the criteria for PB, vPB or PvB and has the highest BCF value based on the outcome of request s 1 and 2 in case it is not possible to conclude that this fraction meets the criterion for T based on the outcome of request 3. If one or more of the relevant fractions are already considered vPvB or PBT, this test is not required.
Long-term toxicity to fish, test method: OECD 210, Fish Early Life Stage Toxicity Test with the relevant fraction that fulfils the criteria for PB, vPB or PvB and has the highest BCF value based on the outcome of requests 1 and 2.

Deadline to submit the requested Information

In the draft decision communicated to you, the time indicated to provide the requested information was 15 months from the date of adoption of the decision if only partition coefficient and water solubility tests were required, 33 months if in addition a persistency test was required, 42 months if in addition a bioaccumulation test was required and 51 months if a *Daphnia reproduction* test was also required. Due to the subsequent changes made in the overall testing strategy and testing required, ECHA adapted the deadlines accordingly to those specified in the body of the decision.

References

[redacted].

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Appendix 2: Procedural history

On the basis of an opinion of the ECHA Member State Committee and due to initial grounds for concern relating to suspected PBT/vPvB properties, exposure of environment and high RCRs, a mixture of: 4-(2,2,3- trimethylcyclopent-3-en- 1-yl)-1-methyl-2-oxabicyclo[2.2.2]octane; 1-(2,2,3- trimethylcyclopent-3-en- 1-yl)-5-methyl-6-oxabicyclo[3.2.1]octane; spiro[cyclohex-3-en-1-yl- [(4,5,6,6a-tetrahydro- 3,6',6',6'a-tetramethyl)- 1,3'(3'aH)- [2H]cyclopenta[b]furan]; spiro[cyclohex-3-en-1-yl- [4,5,6,6a-tetrahydro- 4,6',6',6'a-tetramethyl)- 1,3'(3'aH)- [2H]cyclopenta[b]]furan] (CAS No 426218-78-2, EC No 422-040-1) was included in the Community rolling action plan (CoRAP) for substance evaluation to be evaluated in 2016. The updated CoRAP was published on the ECHA website on 22 March 2016. The competent authority of Spain (hereafter called the evaluating MSCA) was appointed to carry out the evaluation.

In accordance with Article 45(4) of the REACH Regulation, the evaluating MSCA carried out the evaluation of the above substance based on the information in your registration(s) and other relevant and available information.

The evaluating MSCA considered that further information was required to clarify the following concerns: suspected PBT/vPvB properties, high RCR and exposure of environment. Therefore, it prepared a draft decision under Article 46(1) of the REACH Regulation to request further information on suspected PBT/vPvB properties. It subsequently submitted the draft decision to ECHA on 21 March 2017.

The decision making followed the procedure of Articles 50 and 52 of the REACH Regulation as described below.

ECHA notified you of the draft decision and invited you to provide comments.

Registrant(s)' commenting phase

ECHA received comments from you and forwarded them to the evaluating MSCA without delay.

The evaluating MSCA took the comments from you, which were sent within the commenting period, into account and they are reflected in the reasons (Appendix 1). The request(s) and the deadline were amended.

Proposals for amendment by other MSCAs and ECHA and referral to the Member State Committee

The evaluating MSCA notified the draft decision to the competent authorities of the other Member States and ECHA for proposals for amendment.

Subsequently, the evaluating MSCA received proposals for amendment to the draft decision and modified the draft decision. They are reflected in the reasons (Appendix 1).

ECHA referred the draft decision, together with your comments, to the Member State Committee.

ECHA invited you to comment on the proposed amendments.

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Your comments on the proposed amendments were taken into account by the Member State Committee.

MSC agreement seeking stage

The Member State Committee reached a unanimous agreement on the draft decision during its MSC-58 meeting and ECHA took the decision according to Article 52(2) and 51(6) of the REACH Regulation.

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Appendix 3: Further information, observations and technical guidance

1. This decision does not imply that the information provided by you in the registration(s) is in compliance with the REACH requirements. The decision neither prevents ECHA from initiating compliance checks on your dossier(s) at a later stage, nor does it prevent a subsequent decision under the current substance evaluation or a new substance evaluation process once the present substance evaluation has been completed.

2. Failure to comply with the request(s) in this decision, or to otherwise fulfil the information requirement(s) with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In relation to the required experimental study/ies, the sample of the substance to be used ('test material') has to have a composition that is within the specifications of the substance composition that are given by all registrant(s) when testing with the wohole substance is required. Where testing is required for a specific constituent of the registered substance the requirements of the test material as described in Appendix 1 in this decision must be followed. It is the responsibility of all the as registrant(s) to agree on the tested material to be subjected to the test(s) subject to this decision and to document the necessary information on the composition of the test material. The substance identity information of the registered substance and of the sample tested must enable the evaluating MSCA and ECHA to confirm the relevance of the testing for the substance subject to substance evaluation.

4. In relation to the experimental stud(y/ies) the legal text foresees the sharing of information and costs between registrant(s) (Article 53 of the REACH Regulation). You are therefore required to make every effort to reach an agreement regarding each experimental study for every endpoint as to who will carry out the study on behalf of the other registrant(s) and to inform ECHA accordingly within 90 days from the date of this decision under Article 53(1) of the REACH Regulation. This information should be submitted to ECHA using the following form stating the decision number above at:
https://comments.echa.europa.eu/comments_cms/SEDraftDecisionComments.aspx

   Further advice can be found at
http://echa.europa.eu/regulations/reach/registration/data-sharing. If ECHA is not informed of such agreement within 90 days, it will designate one of the registrants to perform the stud(y/ies) on behalf of all of them.